

# EXPERT PANEL FOR FRAGRANCE SAFETY MEETING

## Minutes

September 25-27, 2023

New York City

EXPERT PANEL MEMBERS	RIFM STAFF	Guests
Donald Belsito (Chair) Magnus Bruze Amanda Bryant-Friedrich G. Allen Burton, Jr. Maria Dagli (Vice-Chair) Wolfgang Dekant, virtual only Allison Fryer Trevor Penning I Glenn Sipes Yoshiki Tokura	Anne Marie Api Danielle Botelho Leah Jones Kaushal Joshi (9/26) Aurelia Lapczynski (9/25-26) Isabelle Lee (9/26-27) Holger Moustakas (9/25-27) Jake Muldoon (9/25) Gretchen Ritacco (9/25) Nikaeta Sadekar (9/27) Gary Sullivan (9/25)	Debra Laskin (9/25-27) Cronan McNamara (9/25, am) Robert Weinstein (9/26, am) Paul Thomas (9/26, am) Scot Belanger (9/26) Heather Summers (9/26, pm)

### 1) Discussion of the Meeting Schedule and Agenda Topics

- a) Completion/Signing of the Conflict-of-Interest Statement

Dr. Belsito opened the meeting. The Conflict-of-Interest Statement was signed.

### 2) Minutes

The minutes from the May 2023 meeting were approved with no changes.

### 3) Follow-Up and Informational Items

- a) Follow-Up List

Dr. Api went through the follow-up list and provided updates on items and general comments where applicable.

### 4) Standing Items (For Expert Panel information only; per Panel's request)

- a) RIFM Publications

The Panel reviewed the RIFM publication list. This is a standing item on the agenda, which provides a summary of all RIFM's recent publications.

- b) RIFM Safety Assessment Publications

The Panel reviewed the RIFM safety assessment publications list. This list is an ongoing list of all the published safety assessments.

## 5) RIFM Communication

### a) Update on RIFM

Dr. Api provided an overview of RIFM activities (see Attachment 1).

### b) Communications Update

Mr. Sullivan provided an update on the RIFM communication plans, safety assessment publications, and the Fragrance Resource Center website (see Attachment 2).

### c) Communicating risk and safety

The Panel had a discussion on the best ways to communicate risk and safety.

## 6) RIFM Safety Evaluation Process

### a) Presentation RIFM by D. Botelho Safety Assessment Update and Metrics

Dr. Botelho gave a presentation on the progress of the safety assessment program including the safety assessment update and metrics on naturals (see Attachment 3).

### b) Safety Assessment Overview

- i) 15 Total Safety Assessments including 17 Total materials.

## 7) NCS Safety Assessments

### a) General Comments

- i) Photoallergy statement in the summary section

When no photoallergy data are available, the same statement used in the safety assessments on discrete chemicals will be included in the safety assessments on NCS.

- ii) Differences in volatility between read-across analogs and target materials.

Penetration data are more important than volatilization. If reading across from a bigger molecule to the smaller molecule it is acceptable.

- iii) Environmental

The Panel suggested that persistence and bioaccumulative properties for low exposure NCS materials may not be problematic because they are natural volatile and semi-volatile materials. A summary on resins and fatty acids which had targeted testing on some materials would be useful. However, the Panel suggested that a short peer-reviewed paper detailing the rationale for this would be needed.

- iii) UV absorption Proposal

The Panel suggested an investigation into the calculated MEC for a mixture based on the MECs of the ingredients of the mixture. The hypothesis is that the MEC for the mixture will be based on the MEC of the components of the mixture.

### b) Safety Assessment Review

- i) Total NCS Safety Assessments: 32

Material ID	RIFM ID	Material Name	Tab	Status
1048387	275-E2.1	Peppermint absolute	<b>Tab 16</b>	Insufficient data (photo in testing, genotoxicity in testing, skin resins, enviro resins)
1043845	83-E2.12	Mentha citrata oil	<b>Tab 17</b>	Approved - hold (skin)

Material ID	RIFM ID	Material Name	Tab	Status
1046092	419-E2.12	Pennyroyal oil, Europe	<b>Tab 18</b>	Insufficient data - genotoxicity in test
1045346	771-E2.12	Spearmint oil	<b>Tab 19</b>	Insufficient data – genotoxicity, skin, environment
1043639	5603-E2.12	Spearmint oil, Scotch	<b>Tab 20</b>	Insufficient data – environment
1047048	275-E2.12	Peppermint oil	<b>Tab 21</b>	Insufficient data (photo and genotoxicity in test)
1048457	771-E2.1	Spearmint absolute	<b>Tab 22</b>	Insufficient data (photo and genotoxicity and skin in test)
1045355	272-E2.12	Pine needle oil	<b>Tab 23</b>	Insufficient data – skin sensitization
1044400	645-E2.12	Pine needle, dwarf, oil	<b>Tab 24</b>	Insufficient data – environment
1048354	938-E2.12	Pine oil	<b>Tab 25</b>	Insufficient data – skin sensitization
1046096	646-E2.12	Pine Scotch, oil	<b>Tab 26</b>	Insufficient data - environment
1048582	646-E2.26	Pine Scotch, resinoid	<b>Tab 27</b>	Insufficient data – environment, skin sensitization and genotoxicity and photo may need testing pending outcome of final composition
1044750	5607-E2.12	Pine, Pinus pinaster, oil	<b>Tab 28</b>	Insufficient data - photo and environment
1047095	5501-E2.12	Pine, Pinus pumila, oil	<b>Tab 29</b>	Approved with changes - hold
1044749	1068-E2.12	Pinus nigra oil	<b>Tab 30</b>	Approved - hold
1044761	317-K2.12	Turpentine oil	<b>Tab 31</b>	Insufficient data - hold for clarification from task force
1048580	646-E2.1	Pine Scotch, absolute	<b>Tab 32</b>	Insufficient data - photo in test, skin sensitization needs testing and hold for clarification from task force
1049936	5532-F2.1	Lavandin abrialis absolute	<b>Tab 33</b>	Insufficient data - photo and genotoxicity in test and hold for clarification from task force
1048554	5532-F2.11	Lavandin abrialis	<b>Tab 34</b>	Approved - hold
1044314	5532-F2.12	Lavandin abrialis oil	<b>Tab 35</b>	Approved - hold
1042713	190-F2.1	Lavandin absolute	<b>Tab 36</b>	Insufficient data - genotoxicity
1048557	5533-F2.11	Lavandin grosso	<b>Tab 37</b>	Approved - hold
1048556	5533-F2.1	Lavandin grosso absolute	<b>Tab 38</b>	Insufficient data - photo and genotoxicity in test
1049826	5533-F2.27	Lavandin grosso CO2 extract	<b>Tab 39</b>	Insufficient data - genotoxicity in test
1044315	5533-F2.12	Lavandin grosso oil	<b>Tab 40</b>	Insufficient data - genotoxicity, environment in test
1045551	190-F2.12	Lavandin oil	<b>Tab 41</b>	Insufficient data - genotoxicity in test
1042078	169-F2.1	Lavender absolute	<b>Tab 42</b>	Insufficient data - genotoxicity in test
1049827	169-F2.27	Lavender CO2 extract	<b>Tab 43</b>	Approved - hold
1042646	169-F2.7	Lavender concrete	<b>Tab 44</b>	Insufficient data - genotoxicity and photo in test

Material ID	RIFM ID	Material Name	Tab	Status
1044378	169-F2.12	Lavender oil	<b>Tab 45</b>	Insufficient data - genotoxicity in test, environment needs test
1048647	1095-F2.12	Lavender oil	<b>Tab 46</b>	Insufficient data - genotoxicity, photo, and environment in test
1046844	301-F2.12	Spike lavender oil	<b>Tab 47</b>	Insufficient data - genotoxicity and environment in test

### 8) Presentation Dr. Debra Laskin, Rutgers University Ernest Mario School of Pharmacy, Tuesday morning

Dr. Laskin gave a presentation about her research work (see Attachment 4).

### 9) Presentation by Dr. R. Weinstein

Dr. Robert Weinstein provided an overview of the RIFM strategy sessions and reinforced the Board's commitment to support RIFM. He departed after his presentation.

### 10) Review Safety Assessments Batch 1

CAS #	Material Name	Tab	Status
57345-19-4	Dodecahydro-3,8,8,11a-tetramethyl-5H-3,5a-epoxynaphth[2,1-c]oxepin	<b>Tab 48</b>	Approved
13679-70-4	5-Methyl-2-thiophenecarboxaldehyde	<b>Tab 49</b>	Approved
23950-98-3	Cyclohexanol, 2-methoxy-4-propyl-	<b>Tab 50</b>	Approved with changes (genotoxicity)
120-11-6	Isoeugenyl benzyl ether	<b>Tab 51</b>	Approved with changes (skin)
120-24-1	Isoeugenyl phenylacetate	<b>Tab 52</b>	Approved
710-40-7	pyridine, 5-hexyl-2-methyl-	<b>Tab 53</b>	Approved
137-06-4	o-Toluenethiol	<b>Tab 54</b>	Approved
188417-26-7	Ethyl vanillin isobutyrate	<b>Tab 55</b>	Approved
17369-60-7	5-Ethyl-2,3,4,5-tetramethylcyclohexen-1-one	<b>Tab 56</b>	Approved
68845-35-2	Triethyltrimethyl-2-cyclohexen-1-one	<b>Tab 57</b>	Approved
154171-77-4; 154171-76-3	Spiro[1,3-dioxolane-2,8'(5'H)-[2H-2,4a]methanonaphthalene],hexahydro-1',1',5',5'-tetramethyl-, [2'S-(2'.alpha.,4'a.alpha.,8'a.alpha.)]-	<b>Tab 58</b>	Approved
103-60-6	2-Phenoxyethyl isobutyrate	<b>Tab 59</b>	Approved
128489-02-1; 128489-04-3	Phenol, 4-(3,6-dihydro-4-methyl-2H-pyran-2-yl)-2-methoxy-	<b>Tab 60</b>	Approved
22884-95-3	Benzonitrile, 3,4-dimethyl-	<b>Tab 61</b>	Approved with changes (genotoxicity)
23986-74-5	(-)-Germacrene D	<b>Tab 62</b>	Approved

### 11) Review Safety Assessments Maintenance Batch (Tab 63)

CAS#	Material Name	Tab	Status
7306-12-9	3-Phenyl-3-buten-1-yl acetate	<b>Tab 64</b>	Approved with changes (genotoxicity)
71660-03-2	cis- and trans-p-1(7),8-Menthadien-2-yl acetate	<b>Tab 65</b>	Approved

CAS#	Material Name	Tab	Status
111-81-9	Methyl undec-10-enoate	Tab 66	Approved with changes (genotoxicity, skin, chemistry)
692-86-4	Ethyl 10-undecenoate	Tab 67	Approved with changes (genotoxicity, skin, chemistry)
109-42-2	Butyl 10-undecenoate	Tab 68	Approved with changes (genotoxicity, skin, chemistry)
115-18-4	2-Methyl-3-buten-2-ol	Tab 69	Approved
65405-77-8	cis-3-hexenyl salicylate	Tab 70	Approved hold (approved as is but hold publication for new data coming soon)

## 12) Review Safety Assessments Batch

CAS#	Material Name	Tab	Status
78-59-1	Isophorone	Tab 71	Hold – more data analysis
89-81-6; 6091-50-5; 4573-50-6	Piperitone	Tab 72	Approved with changes - HOLD more data analysis
1193-18-6	3-methyl-2-cyclohexen-1-one	Tab 73	Hold - more data analysis
3720-16-9	3-methyl-5-propyl-2-cyclohexen-1-one	Tab 74	Hold - more data analysis

Dr. Joshi gave a presentation summarizing the data on isophorone (see Attachment 5). The safety assessments will be revised and updated and reviewed again by the core team and brought to the Expert Panel for a final decision.

## 13) Benzophenone, CAS 119-61-9

The Panel recommended that UV absorption be conducted on analytical grade benzophenone. A photo-GARD assay and a photo-DPR may be needed on the pure material. It was recommended that the material be stored in the dark and under nitrogen.

## 14) RIFM Research Projects

- a) Overview of research programs

Dr. Api provided an overview of the research programs conducted by RIFM.

- b) Epidemiology

Dr. Bruze reported that the EDEN group has not been active due to the pandemic. However, they will meet on June 12 to continue their evaluation of all the data from the study.

- c) Creme RIFM Aggregate Exposure Model

### i) Presentation by Dr. Cronan McNamara, Creme Global, Monday, Sept. 25 AM

Dr. McNamara gave an update on the Creme RIFM Aggregate Exposure Model and detailed the most recent changes and updates to the model (See Attachment 6).

- d) Chemistry

### i) Presentation of chemistry video

Dr. Moustakas presented the RIFM Video on chemistry that was recently completed. The video is available on the RIFM YouTube Channel <https://youtu.be/6h4WRBZ6lc?si=bqF1171HUbkyrmYe>. The video is available for use by members and will be part of a communication plan.

ii) **Chemical Signature paper**

Drs. Moustakas and Muldoon gave an update on the next chemical grouping paper that is planned (See Attachment 7).

e) **Environmental Research Program Update**

i) **Presentation by P. Thomas, Kreatis “A Project to Identify Toxicity of a Highly Complex Mixture and to Simulate the Results in silico: Main results and difficulties met during the project.”**

Dr. Thomas presented an update on the Project to Identify Toxicity of a Highly Complex Mixture and to Simulate the Results in silico (**see Attachment 8**).

ii) **Presentation by S. Belanger on OTNE species sensitivity**

Dr. Belanger gave a presentation on how species sensitivity distribution was developed and how it can be used for environmental risk assessment (**see Attachment 9**).

iii) **Presentation by Heather Summers, Integral on Framework 2**

Ms. Summers gave a presentation on the updated environmental framework now called “Framework 2” (**see Attachment 10**). The Panel congratulated Ms. Lapczynski and Summers on a job well-done and encouraged the completion of the manuscript for publication as soon as possible. The Panel commented that this project is another example of next generation predictive toxicology, guided and developed by research and used for practical applications.

f) **Skin Sensitization Research Projects**

i) **Presentation by I. Lee/H. Moustakas on epoxide research update**

Drs. Lee and Moustakas gave a presentation updating the Panel on the epoxide research project (**see Attachment 11**).

g) **Phototoxicity and Photoallergy**

Ms. Ritacco provided an update on the phototoxicity and photoallergy research projects.

h) **Repeat Dose Toxicity**

Dr. Joshi provided an update on the repeat dose and reproduction research projects; the plan is to have a presentation of the IONTOX data at the next Expert Panel meeting.

i) **Respiratory**

Dr. Sadekar provided an update on the respiratory research projects.

## 15) New Expert Panel Members

The Panel discussed potential new Panel members.

## 16) Panel Executive Session

The Panel held an Executive Session and invited Dr. Laskin to join the Panel as a member. Dr. Laskin was pleased to accept the invitation.

## 17) Future Meeting Dates

- Monday-Wednesday, Jan. 22-24, 2024, San Diego, CA

- Monday-Wednesday, May 20-22, 2024, Edinburgh
- Monday-Wednesday, September 23-25, 2024, New Jersey
- Monday-Wednesday, January 27-29, 2025 ?
- Monday-Wednesday, May 19-21, 2025, Krakow, Poland
- Monday-Wednesday, Sept. 29- Oct. 1, 2025, NY/NJ

Respectfully submitted,



Anne Marie Api, Ph.D., ATS  
President

- Attachment 1: Presentation: Dr. Anne Marie Api
- Attachment 2: Presentation: Mr. Gary Sullivan
- Attachment 3: Presentation: Dr. Danielle Botelho
- Attachment 4: Presentation: Dr. Debra Laskin
- Attachment 5: Presentation: Dr. Kaushal Joshi
- Attachment 6: Presentation: Dr. Cronin McNamara
- Attachment 7: Presentation: Drs. Holger Moustakas and Jake Muldoon
- Attachment 8: Presentation: Dr. Paul Thomas
- Attachment 9: Presentation: Dr. Scott Belanger
- Attachment 10: Presentation: Ms. Heather Summers
- Attachment 11: Presentation: Drs. Isabelle Lee and Holger Moustakas